

NEWS RELEASE

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Scientists Identify Genes That May be Key to Human “Arms Race” with Malaria

FOR IMMEDIATE RELEASE

Scientists at North Carolina State University have taken an important step toward identifying specific genes within the parasite that causes the deadliest form of malaria – genes that could be the key to developing vaccines and drug treatments that are urgently needed to save lives.

Dr. Philip Awadalla, assistant professor of genetics, and NC State colleagues Kate McGee and John Keebler, along with researchers from the National Institutes of Health and Oxford University, looked at more than 3,500 genes within the genome of *Plasmodium falciparum* – the parasite responsible for malaria – and identified several genes that most likely have to do with how the disease affects human beings.

The scientists published their results in the Dec. 10 online edition of *Nature Genetics*.

The genome of *P. falciparum* had previously been sequenced, giving scientists a broad overview of its structure, but they lacked specific information about the function of genes within the genome that might control the way the organism interacts with its host’s immune system. In order to find likely candidates, Awadalla and his colleagues studied different samples of the same organism, looking for what are known as polymorphisms – locations along the genome where specific genes differ between the samples.

“All organisms change over time, and these genetic mutations fall into two major categories,” Awadalla says. “One type of mutation you see is called a selective sweep – where every sample of an organism shows the same change. These are adaptive mutations which sweep through the population rapidly removing all other mutations at that gene.

“But when you’re dealing with an organism that’s trying to stay one step ahead of new drug therapies, you tend to see an accumulation of variation among samples. So rather than a selective sweep, in which everyone gets the mutation or new trait, you see more individual

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mutations because of constant turnover in both the parasite and the host – an “arms race” of sorts between the human immune system and the parasite.”

To pinpoint the arms race genes, the scientists did a general survey of the *P. falciparum* genome and identified sites on the genome that displayed a high degree of variation, or polymorphism. They took the genes from these sites and used bacteria to express the proteins that these genes would normally produce inside the parasite, then tested these proteins against human immunity proteins to see if they would react. A positive reaction with the human immunity proteins indicated that the genes would be good candidates for drug and vaccine targets.

Awadalla and the team identified 100 highly variable genes within the *P. falciparum* genome. Of those 100, 10 new genes of previously unknown function showed strong reactions to the human immunity protein, giving the scientists a clue to their function, and a starting point for further research into how malaria targets the human body and its effect on the immune system.

“The question now is to find out exactly what these genes do, and to determine how these genetic variants work,” says Awadalla. “Then hopefully we’ll be able to tailor a drug or vaccine that will interact with the proteins that the genes produce. In the short term, we’ll be able to identify both malarial and human mutations that are important in stopping this disease.”